

JPW

## PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: JOHN P. WHITE  
COOPER & DUNHAM LLP  
1185 AVENUE OF THE AMERICAS  
NEW YORK NY 10036

OCT 17 2001

PCT

M  
NOTIFICATION OF TRANSMITTAL OF  
INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing  
(day/month/year)

12 OCT 2001

Applicant's or agent's file reference

58332-A-PCT

International application No.

PCT/US00/16594

International filing date (day/month/year)

15 JUNE 2000

Priority Date (day/month/year)

J 15 JUNE 1999

Applicant

THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK

## IMPORTANT NOTIFICATION

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

## 4. REMINDER

*12/15/2001 SMC*

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231  
Facsimile No. (703) 305-3230

Authorized officer  
GERALD R. EWOLDT  
Telephone No. (703) 308-0196

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

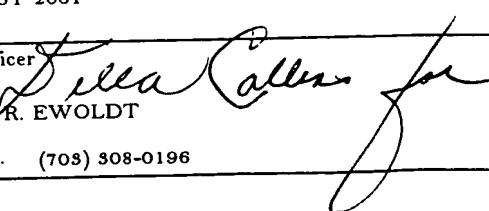
(PCT Article 36 and Rule 70)

|  |  |  |
|--|--|--|
| Applicant's or agent's file reference<br>58332-A-PCT   | FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |  |
| International application No.<br>PCT/US00/16594  | International filing date (day/month/year)<br>15 JUNE 2000   | Priority date (day/month/year)<br>15 JUNE 1999 |
| International Patent Classification (IPC) or national classification and IPC<br>Please See Supplemental Sheet. |  |  |
| Applicant<br>THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK                                       |  |  |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets.
 

This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 4 sheets.
3. This report contains indications relating to the following items:
  - I  Basis of the report
  - II  Priority
  - III  Non-establishment of report with regard to novelty, inventive step or industrial applicability
  - IV  Lack of unity of invention
  - V  Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability, citations and explanations supporting such statement
  - VI  Certain documents cited
  - VII  Certain defects in the international application
  - VIII  Certain observations on the international application

|  |   |
|--|---|
| Date of submission of the demand<br>15 JANUARY 2001  | Date of completion of this report<br>29 AUGUST 2001                                   |
| Name and mailing address of the IPEA/US<br>Commissioner of Patents and Trademarks<br>Box PCT<br>Washington, D.C. 20231 | Authorized officer<br>GERALD R. EWOLDT<br>Telephone No. (703) 308-0196                |
| Facsimile No. (703) 305-3290   |  |

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/16594

## I. Basis of the report

## 1. With regard to the elements of the international application:\*

 the international application as originally filed the description:

pages \_\_\_\_\_ 1-119

pages \_\_\_\_\_ NONE

pages \_\_\_\_\_ NONE

pages \_\_\_\_\_ , filed with the letter of \_\_\_\_\_

 the claims:

pages \_\_\_\_\_ 120-131

pages \_\_\_\_\_ NONE

pages \_\_\_\_\_ NONE

pages \_\_\_\_\_ , filed with the letter of \_\_\_\_\_

 the drawings:

pages \_\_\_\_\_ 1-44

pages \_\_\_\_\_ NONE

pages \_\_\_\_\_ , filed with the letter of \_\_\_\_\_

 the sequence listing part of the description:

pages \_\_\_\_\_ NONE

pages \_\_\_\_\_ NONE

pages \_\_\_\_\_ , filed with the letter of \_\_\_\_\_

pages \_\_\_\_\_ , filed with the letter of \_\_\_\_\_

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which

the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

 the language of a translation furnished for the purposes of international search (under Rule 23.1(b)). the language of publication of the international application (under Rule 48.3(b)). the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

 contained in the international application in printed form. filed together with the international application in computer readable form. furnished subsequently to this Authority in written form. furnished subsequently to this Authority in computer readable form. The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished. The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.4.  The amendments have resulted in the cancellation of: the description, pages \_\_\_\_\_ NONE the claims, Nos. \_\_\_\_\_ NONE the drawings, sheets/fig. \_\_\_\_\_ NONE5.  This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\*Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been and will not be examined in respect of:

the entire international application.

claims Nos. 49

because:

the said international application, or the said claim Nos. relate to the following subject matter which does not require international preliminary examination (*specify*).

the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 49 are so unclear that no meaningful opinion could be formed (*specify*).

There is no antecedent basis for the recitation of "MIR" in the claim.

the claims, or said claims Nos.    are so inadequately supported by the description that no meaningful opinion could be formed.

no international search report has been established for said claims Nos.   .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

the written form has not been furnished or does not comply with the standard.

the computer readable form has not been furnished or does not comply with the standard.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/16594

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. statement****Novelty (N)**

|        |                    |     |
|--------|--------------------|-----|
| Claims | <u>NONE</u>        | YES |
| Claims | <u>1-48, 50-56</u> | NO  |

**Inventive Step (IS)**

|        |                    |     |
|--------|--------------------|-----|
| Claims | <u>NONE</u>        | YES |
| Claims | <u>1-48, 50-56</u> | NO  |

**Industrial Applicability (IA)**

|        |                    |     |
|--------|--------------------|-----|
| Claims | <u>1-48, 50-56</u> | YES |
| Claims | <u>NONE</u>        | NO  |

**2. citations and explanations (Rule 70.7)**

Claims 1-48 and 50-56 lack novelty under PCT Article 33(2) as being anticipated by Jiang et al.

The Jiang et al reference teaches a method for generating CD8+CD28- suppressor T cells. Jiang et al teaches obtaining peripheral blood T cells from a subject and stimulating the cells in vitro multiple times with antigenic peptide to establish T cell lines (page 691, second column in particular). Jiang et al further teaches isolating CD4+ and CD8+ T cells from the generated lines and further isolating CD8+CD28- T cells (page 691, second column in particular). Jiang et al further teaches the testing of the CD8+CD28- T cells for their suppressive effect on the CD4+ cells (page 692, second column through page 694, first column in particular). Jiang et al also teaches expansion of the CD8+CD28- T cells for five generations in vitro and their maintenance of suppressive effect through those generations (page 694 in particular). While the working example in the Jiang et al reference is a cell system directed at tetanus toxoid reactivity, not an alloantigen, the reference expresses previous personal success with the in vitro generation of allospecific suppressor T cells (page 690, second column in particular). Further, since the T cells and antigen are derived from different species of organisms, the showing of Jiang et al fully qualifies as demonstrating xenospecific success. The Jiang et al reference further teaches that the findings reported in the reference have direct relevance to allo- and xenogeneic reactivity, as well as the treatment of autoimmune disease due to the fact that the cells can be educated ex vivo with suppressogenic peptides (page 698, first column in particular). The prior art teaching anticipates the claimed invention.

Claims 4, 8, 11 and 27-32 lack novelty under PCT Article 33(2) as being anticipated by Liu et al.

The Liu et al reference teaches allogeneic and xenogeneic CD8+CD28- suppressor T cells (Abstract and paragraph bridging pages 782-783 in particular). While Liu et al does not teach the same method of isolation as that recited in the claim, it is noted that the claim is written in a product-by-process format, IE the claim is a compound claim drawn to the cells, but recites (Continued on Supplemental Sheet.)

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US98/16594

**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

**CLASSIFICATION:**

The International Patent Classification (IPC) and/or the National classification are as listed below:  
IPC(7): A01N 63/00; C12N 5/02, 5/06, 5/08 and US Cl.: 424/93.71, 810; 435/325, 372.3, 373, 374, 377

**V. 2. REASoNED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):**

V. 2. REASoNED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):  
a preferred method of obtaining those cells. Since there is no disclosed special property attributable to the CD8+CD28- cells obtained by the instant method to distinguish the cells from those of the prior art, the instant cells are seen as the same as those of the Liu et al reference. The prior art teaching anticipates the claimed invention.

Claims 1-48 and 50-56 meet the criteria set out in PCT Article 33(4) for industrial applicability because it is highly desired in the art to develop methods of immunosuppression which can specifically target an antigen-specific response without general immunosuppression of the subject.

**----- NEW CITATIONS -----**

LIU et al. Specific suppression of T helper alloreactivity by allo-MHC class I-restricted CD8+CD28- T cells. International Immunology. June 1998, Vol. 10, No. 6, pages 775-783, see entire document.

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: JOHN P. WHITE  
COOPER & DUNHAM LLP  
1185 AVENUE OF THE AMERICAS  
NEW YORK NY 10036

# PCT

## WRITTEN OPINION

(PCT Rule 66)

|   |   |   |   |
|---|---|---|---|
|   |   | Date of Mailing<br>(day/month/year)                   | 18 MAY 2001   |
| Applicant's or agent's file reference<br><b>58332-A-PCT</b>   |   | REPLY DUE   | within TWO months<br>from the above date of mailing |
| International application No.<br><b>PCT/US00/16594</b>  | International filing date (day/month/year)<br><b>15 JUNE 2000</b> | Priority date (day/month/year)<br><b>15 JUNE 1999</b> |   |
| International Patent Classification (IPC) or both national classification and IPC<br>Please See Supplemental Sheet. |   |   |   |
| Applicant<br><b>THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK</b>                                     |   |   |   |

1. This written opinion is the first (first, etc.) drawn by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

- I  Basis of the opinion
- II  Priority
- III  Non-establishment of opinion with regard to novelty, inventive step or industrial applicability
- IV  Lack of unity of invention
- V  Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI  Certain documents cited
- VII  Certain defects in the international application
- VIII  Certain observations on the international application

3. The applicant is hereby invited to reply to this opinion.

**When?** See the time limit indicated above. ~~The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).~~

**How?** By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

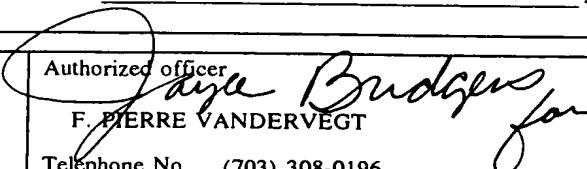
**Also** For an additional opportunity to submit amendments, see Rule 66.4.

For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.

For an informal communication with the examiner, see Rule 66.6.

**If no reply is filed**, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 15 OCTOBER 2001.

|  |   |
|--|---|
| Name and mailing address of the IPEA/US<br>Commissioner of Patents and Trademarks<br>Box PCT<br>Washington, D.C. 20231 | Authorized officer<br><br>F. PIERRE VANDER VEGT |
| Facsimile No. (703) 305-3230   | Telephone No. (703) 308-0196  |

## WRITTEN OPINION

International application No.

PCT/US00/16594

**I. Basis of the opinion**1. With regard to the **elements of the international application**\*: the international application as originally filed the description:pages 1-119, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_ the claims:pages 120-131, as originally filed  
pages NONE, as amended (together with any statement) under Article 19  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_ the drawings:pages 1-44, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_ the sequence listing part of the description:pages NONE, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.  
These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is: the language of a translation furnished for the purposes of international search (under Rule 23.1(b)). the language of publication of the international application (under Rule 48.3(b)). the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the written opinion was drawn on the basis of the sequence listing: contained in the international application in printed form. filed together with the international application in computer readable form. furnished subsequently to this Authority in written form. furnished subsequently to this Authority in computer readable form. The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished. The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.4.  The amendments have resulted in the cancellation of: the description, pages NONE the claims, Nos. NONE the drawings, sheets/fig NONE5.  This opinion has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed".

## WRITTEN OPINION

International application No.  
PCT/US00/16594**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been and will not be examined in respect of:

the entire international application.

claims Nos. 49

because:

the said international application, or the said claim Nos.    relate to the following subject matter which does not require international preliminary examination (*specify*).

the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 49 are so unclear that no meaningful opinion could be formed (*specify*).

There is no antecedent basis for the recitation of "MIR" in the claim.

the claims, or said claims Nos.    are so inadequately supported by the description that no meaningful opinion could be formed.

no international search report has been established for said claims Nos. 49.

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

the written form has not been furnished or does not comply with the standard.

the computer readable form has not been furnished or does not comply with the standard.

## WRITTEN OPINION

International application No.

PCT/US00/16594

**V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. statement**

|                               |                           |     |
|-------------------------------|---------------------------|-----|
| Novelty (N)                   | Claims <u>NONE</u>        | YES |
|                               | Claims <u>1-48, 50-56</u> | NO  |
| Inventive Step (IS)           | Claims <u>NONE</u>        | YES |
|                               | Claims <u>1-48, 50-56</u> | NO  |
| Industrial Applicability (IA) | Claims <u>1-48, 50-56</u> | YES |
|                               | Claims <u>NONE</u>        | NO  |

**2. citations and explanations**

Claims 1-48 and 50-56 lack novelty under PCT Article 33(2) as being anticipated by Jiang et al.

The Jiang et al reference teaches a method for generating CD8+CD28- suppressor T cells. Jiang et al teaches obtaining peripheral blood T cells from a subject and stimulating the cells in vitro multiple times with antigenic peptide to establish T cell lines (page 691, second column in particular). Jiang et al further teaches isolating CD4+ and CD8+ T cells from the generated lines and further isolating CD8+CD28- T cells (page 691, second column in particular). Jiang et al further teaches the testing of the CD8+CD28- T cells for their suppressive effect on the CD4+ cells (page 692, second column through page 694, first column in particular). Jiang et al also teaches expansion of the CD8+CD28- T cells for five generations in vitro and their maintenance of suppressive effect through those generations (page 694 in particular). While the working example in the Jiang et al reference is a cell system directed at tetanus toxoid reactivity, not an alloantigen, the reference expresses previous personal success with the in vitro generation of allospecific suppressor T cells (page 690, second column in particular). Further, since the T cells and antigen are derived from different species of organisms, the showing of Jiang et al fully qualifies as demonstrating xenospecific success. The Jiang et al reference further teaches that the findings reported in the reference have direct relevance to allo- and xenogeneic reactivity, as well as the treatment of autoimmune disease due to the fact that the cells can be educated ex vivo with suppressogenic peptides (page 698, first column in particular). The prior art teaching anticipates the claimed invention.

Claims 4, 8, 11 and 27-32 lack novelty under PCT Article 33(2) as being anticipated by Liu et al.

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**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

**TIME LIMIT:**

The time limit set for response to a Written Opinion may not be extended. 37 CFR 1.484(d). Any response received after the expiration of the time limit set in the Written Opinion will not be considered in preparing the International Preliminary Examination Report.

**CLASSIFICATION:**

The International Patent Classification (IPC) and/or the National classification are as listed below:

IPC(7): A01N 63/00; C12N 5/02, 5/06, 5/08 and US Cl.: 424/93.71, 810; 435/325, 372.3, 373, 374, 377

**V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):**

is noted that the claim is written in a product-by-process format, IE the claim is a compound claim drawn to the cells, but recites a preferred method of obtaining those cells. Since there is no disclosed special property attributable to the CD8 + CD28- cells obtained by the instant method to distinguish the cells from those of the prior art, the instant cells are seen as the same as those of the Liu et al reference. The prior art teaching anticipates the claimed invention.

Claims 1-48 and 50-56 meet the criteria set out in PCT Article 33(4) for industrial applicability because it is highly desired in the art to develop methods of immunosuppression which can specifically target an antigen-specific response without general immunosuppression of the subject.

**----- NEW CITATIONS -----**

LIU et al. Specific suppression of T helper alloreactivity by allo-MHC class I-restricted CD8 + CD28- T cells. International Immunology. June 1998, Vol. 10, No. 6, pages 775-783, see entire document.

The demand must be filed directly with the competent International Preliminary Examining Authority or, if two or more Authorities are competent, with the one chosen by the applicant. The full name or two-letter code of that Authority may be indicated by the applicant on the line below:

IPEA/ US

# PCT

## CHAPTER II

### DEMAND

under Article 31 of the Patent Cooperation Treaty:

The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty.

For International Preliminary Examining Authority use only

Identification of IPEA

Date of receipt of DEMAND

| Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION  |  | Applicant's or agent's file reference<br>58332-A-PCT                                 |
|--|--|--|
| International application No.<br>PCT/US00/16594  | International filing date (day/month/year)<br>15 June 2000 | (Earliest) Priority date (day/month/year)<br>15 June 1999                            |
| Title of invention<br>GENERATION OF ANTIGEN SPECIFIC T SUPPRESSOR CELLS FOR<br>TREATMENT OF REJECTION  |  |  |
| Box No. II APPLICANT(S)  |  |  |
| Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)<br><br>THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY<br>OF NEW YORK<br>West 116th Street and Broadway<br>New York, New York 10027<br>United States of America |  | Telephone No.:<br>None<br><br>Facsimile No.:<br>None<br><br>Teleprinter No.:<br>None |
| State (i.e. country) of nationality:<br>United States of America   |  | State (i.e. country) of residence:<br>United States of America                       |
| Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)<br><br>SUCIU-FOCA, Nicole<br>120 Central Park South<br>Apt. 19A<br>New York, New York 10019<br>United States of America   |  |  |
| State (i.e. country) of nationality:<br>United States of America   |  | State (i.e. country) of residence:<br>United States of America                       |
| Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)<br><br>CORTESINI, Raffaello<br>120 Central Park South<br>Apt. 19A<br>New York, New York 10019<br>United States of America                                       |  |  |
| State (i.e. country) of nationality:<br>Italy  |  | State (i.e. country) of residence:<br>United States of America                       |
| <input checked="" type="checkbox"/> Further applicants are indicated on a continuation sheet.  |  |  |

## Continuation of Box No. II APPLICANT(S)

*If none of the following sub-boxes is used, this sheet is not to be included in the demand.*

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

LIU, Zhuoru  
 100 Haven Avenue  
 Apt. 9C  
 New York, New York 10032  
 United States of America

State (i.e. country) of nationality:  
 United States of America

State (i.e. country) of residence:  
 United States of America

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

CHANG, Chih-Chao  
 555 Central Park Avenue  
 Apt. 228  
 Scarsdale, New York 10583  
 United States of America

State (i.e. country) of nationality:  
 United States of America

State (i.e. country) of residence:  
 United States of America

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

State (i.e. country) of nationality:

State (i.e. country) of residence:

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

State (i.e. country) of nationality:

State (i.e. country) of residence:

Further applicants are indicated on another continuation sheet.

**Box No. III AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE**

The following person is  agent  common representative

and  has been appointed earlier and represents the applicant(s) also for international preliminary examination.

is hereby appointed and any earlier appointment of (an) agent(s)/common representative is hereby revoked.

is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.

Name and address: (*Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.*)

WHITE, John P.  
Cooper & Dunham LLP  
1185 Avenue of the Americas  
New York, New York 10036  
United States of America

Telephone No.:  
(212) 278-0400

Faximile No.:  
(212) 391-0526

Teleprinter No.:  
None

Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

**Box No. IV STATEMENT CONCERNING AMENDMENTS**

The applicant wishes the International Preliminary Examining Authority\*

- (i)  to start the international preliminary examination on the basis of the international application as originally filed.
- (ii)  to take into account the amendments under Article 34 of
  - the description (amendments attached).
  - the claims (amendments attached).
  - the drawings (amendments attached).
- (iii)  to take into account any amendments of the claims under Article 19 filed with the International Bureau (a copy is attached).
- (iv)  to disregard any amendments of the claims made under Article 19 and to consider them as reversed.
- (v)  to postpone the start of the international preliminary examination until the expiration of 20 months from the priority date unless that Authority receives a copy of any amendments made under Article 19 or a notice from the applicant that he does not wish to make such amendments (Rule 69.1(d)). (*This check-box may be marked only where the time limit under Article 19 has not yet expired.*)

\* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

**Box No. V ELECTION OF STATES**

The applicant hereby elects all eligible States (*that is, all States which have been designated and which are bound by Chapter II of the PCT*) except .....

.....

(*If the applicant does not wish to elect certain eligible States, the name(s) or country code(s) of those States must be indicated above.*)

**Box No. VI CHECK LIST**

The demand is accompanied by the following documents for the purposes of international preliminary examination:

1. amendments under Article 34
 

|             |   |        |
|-------------|---|--------|
| description | : | sheets |
| claims      | : | sheets |
| drawings    | : | sheets |
2. letter accompanying amendments under Article 34
 

|   |        |
|---|--------|
| : | sheets |
|---|--------|
3. copy of amendments under Article 19
 

|   |        |
|---|--------|
| : | sheets |
|---|--------|
4. copy of statement under Article 19
 

|   |        |
|---|--------|
| : | sheets |
|---|--------|
5. other (specify):
 

|   |        |
|---|--------|
| : | sheets |
|---|--------|

**For International Preliminary Examining Authority use only**

received      not received

|                          |                          |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |

The demand is also accompanied by the item(s) marked below:

1.  separate signed power of attorney
2.  copy of general power of attorney
3.  statement explaining lack of signature
4.  fee calculation sheet
5.  other (specify): Express Mail Certificate of Mailing Bearing Express Mail Label #EK873630375US dated 16 January 2001

**Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE**

*Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).*




---

 John P. White, Reg. No. 28,678

---

 16 January 2001

---

 Date
**For International Preliminary Examining Authority use only**

1. Date of actual receipt of DEMAND:

2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):

3.  The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5. below, does not apply.  The applicant has been informed accordingly.
4.  The date of receipt of the demand is WITHIN the period of 19 months from the priority date as extended by virtue of Rule 80.5.
5.  Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rule 82.

**For International Bureau use only**

Demand received from IPEA on:

PCT

## REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference  
(if desired) (12 characters maximum) 58332-A-PCT/JPW/EMW
**Box No. I TITLE OF INVENTION GENERATION OF ANTIGEN SPECIFIC T SUPPRESSOR CELLS  
FOR TREATMENT OF REJECTION**
**Box No. II APPLICANT**

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY  
OF NEW YORK  
West 116th Street and Broadway  
New York, New York 10027  
United States of America

 This person is also inventor.

Telephone No.

None

Facsimile No.

None

Teleprinter No.

None

State (that is, country) of nationality:

United States of America

State (that is, country) of residence:

United States of America

This person is applicant for the purposes of:

 all designated States all designated States except the United States of America the United States of America only the States indicated in the Supplemental Box**Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)**

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

SUCIU-FOCA, Nicole  
120 Central Park South  
Apt. 19A  
New York, New York 10019  
United States of America

This person is:

 applicant only applicant and inventor inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

United States of America

State (that is, country) of residence:

United States of America

This person is applicant for the purposes of:

 all designated States all designated States except the United States of America the United States of America only the States indicated in the Supplemental Box Further applicants and/or (further) inventors are indicated on a continuation sheet.**Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE**

The person identified below is hereby has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:

 agent common representative

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

WHITE, John P.  
Cooper & Dunham LLP  
1185 Avenue of the Americas  
New York, New York 10036  
United States of America

Telephone No.

(212) 278-0400

Facsimile No.

(212) 391-0526

Teleprinter No.

None

Address for correspondence: Mark this check-box where no agent or common representative is has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

See Notes to the request form

## Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

*If none of the following sub-boxes is used, this sheet should not be included in the request.*

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

CORTESINI, Raffaello  
120 Central Park South  
Apt. 19A  
New York, New York 10019  
United States of America

This person is:

- applicant only  
 applicant and inventor  
 inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:  
Italy

State (that is, country) of residence:  
United States of America

This person is applicant for the purposes of:  all designated States  all designated States except the United States of America  the United States of America only  the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

LIU, Zhuoru  
100 Haven Avenue  
Apt. 9C  
New York, New York 10032  
United States of America

This person is:

- applicant only  
 applicant and inventor  
 inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:  
United States of America

State (that is, country) of residence:  
United States of America

This person is applicant for the purposes of:  all designated States  all designated States except the United States of America  the United States of America only  the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

CHANG, Chih-Chao  
555 Central Park Avenue  
Apt. 228  
Scarsdale, New York 10583  
United States of America

This person is:

- applicant only  
 applicant and inventor  
 inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:  
United States of America

State (that is, country) of residence:  
United States of America

This person is applicant for the purposes of:  all designated States  all designated States except the United States of America  the United States of America only  the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

This person is:

- applicant only  
 applicant and inventor  
 inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

State (that is, country) of residence:

This person is applicant for the purposes of:  all designated States  all designated States except the United States of America  the United States of America only  the States indicated in the Supplemental Box

Further applicants and/or (further) inventors are indicated on another continuation sheet.

## Box No.V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):

## Regional Patent

- AP ARIPO Patent: GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- EA Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- EP European Patent: AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- OA OAPI Patent: BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)

National Patent (if other kind of protection or treatment desired, specify on dotted line):

- AE United Arab Emirates
  - AL Albania
  - AM Armenia
  - AT Austria
  - AU Australia
  - AZ Azerbaijan
  - BA Bosnia and Herzegovina
  - BB Barbados
  - BG Bulgaria
  - BR Brazil
  - BY Belarus
  - CA Canada
  - CH and LI Switzerland and Liechtenstein
  - CN China
  - CR Costa Rica
  - CU Cuba
  - CZ Czech Republic
  - DE Germany
  - DK Denmark
  - DM Dominica
  - EE Estonia
  - ES Spain
  - FI Finland
  - GB United Kingdom
  - GD Grenada
  - GE Georgia
  - GH Ghana
  - GM Gambia
  - HR Croatia
  - HU Hungary
  - ID Indonesia
  - IL Israel
  - IN India
  - IS Iceland
  - JP Japan
  - KE Kenya
  - KG Kyrgyzstan
  - KP Democratic People's Republic of Korea
  - KR Republic of Korea
  - KZ Kazakhstan
  - LC Saint Lucia
  - LK Sri Lanka
  - LR Liberia
  - LS Lesotho
  - LT Lithuania
  - LU Luxembourg
  - LV Latvia
  - MA Morocco
  - MD Republic of Moldova
  - MG Madagascar
  - MK The former Yugoslav Republic of Macedonia
  - MN Mongolia
  - MW Malawi
  - MX Mexico
  - NO Norway
  - NZ New Zealand
  - PL Poland
  - PT Portugal
  - RO Romania
  - RU Russian Federation
  - SD Sudan
  - SE Sweden
  - SG Singapore
  - SI Slovenia
  - SK Slovakia
  - SL Sierra Leone
  - TJ Tajikistan
  - TM Turkmenistan
  - TR Turkey
  - TT Trinidad and Tobago
  - TZ United Republic of Tanzania
  - UA Ukraine
  - UG Uganda
  - US United States of America
- continuation-in-part (see Page 5)
- UZ Uzbekistan
  - VN Viet Nam
  - YU Yugoslavia
  - ZA South Africa
  - ZW Zimbabwe

Check-boxes reserved for designating States which have become party to the PCT after issuance of this sheet:

- MZ Mozambique
- BZ Belize

**Precautionary Designation Statement:** In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)

See Notes to the request form

**Box No. VI PRIORITY CLAIM** Further priority claims indicated in the Supplemental Box.

| Filing date<br>of earlier application<br>(day/month/year) | Number<br>of earlier application | Where earlier application is:    |  |  |
|---|----------------------------------|----------------------------------|--|--|
|   |                                  | national application:<br>country | regional application:<br>regional Office | international application:<br>receiving Office |
| item (1) 15.06.99<br>(15 June 1999)                       | 09/333,809                       | US                               |  |  |
| item (2)  |                                  |                                  |  |  |
| item (3)  |                                  |                                  |  |  |

The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office) identified above as item(s): 1

\* Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.

**Box No. VII INTERNATIONAL SEARCHING AUTHORITY**

Choice of International Searching Authority (ISA)  
(if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):

ISA / US

Request to use results of earlier search; reference to that search (if an earlier search has been carried out by or requested from the International Searching Authority):

Date (day/month/year)

Number

Country (or regional Office)

**Box No. VIII CHECK LIST; LANGUAGE OF FILING**

This international application contains the following number of sheets:

|   |   |     |
|---|---|-----|
| request                                       | : | 6   |
| description (excluding sequence listing part) | : | 119 |
| claims  | : | 12  |
| abstract                                      | : | 1   |
| drawings                                      | : | 44  |
| sequence listing part of description          | : | 0   |

Total number of sheets : 182

This international application is accompanied by the item(s) marked below:

1.  fee calculation sheet
2.  separate signed power of attorney
3.  copy of general power of attorney: reference number, if any:
4.  statement explaining lack of signature
5.  priority document(s) identified in Box No. VI as item(s):
6.  translation of international application into (language):
7.  separate indications concerning deposited microorganism or other biological material
8.  nucleotide and/or amino acid sequence listing in computer readable form
9.  other (specify): Transmittal Letter, Attachment A

Figure of the drawings which should accompany the abstract:

Language of filing of the international application: English

**Box No. IX SIGNATURE OF APPLICANT OR AGENT**

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK

NAME: Jack M. Granowitz

6/21/00

Date

TITLE: Executive Director, Columbia Innovation Enterprise

For receiving Office use only

|   |  |
|---|--|
| 1. Date of actual receipt of the purported international application:   | 2. Drawings:   |
| 3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application: | <input type="checkbox"/> received:<br><input type="checkbox"/> not received:             |
| 4. Date of timely receipt of the required corrections under PCT Article 11(2):  |  |
| 5. International Searching Authority (if two or more are competent): ISA /  | 6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid. |

For International Bureau use only

|   |
|---|
| Date of receipt of the record copy by the International Bureau: |
|---|

|   |                                  |  |  |  |
|---|----------------------------------|--|--|--|
| <b>Box No. VI PRIORITY CLAIM</b>                          |                                  | <input type="checkbox"/> Further priority claim indicated in the Supplemental Box. |  |  |
| Filing date<br>of earlier application<br>(day/month/year) | Number<br>of earlier application | Where earlier application is:  |  |  |
| item (1) 15.06.99<br>(15 June 1999)                       | 09/333,809                       | national application:<br>country   | regional application:<br>regional Office | international application:<br>receiving Office |
| item (2)  |                                  |  |  |  |
| item (3)  |                                  |  |  |  |

The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office) identified above as item(s): 1

\* Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.

**Box No. VII INTERNATIONAL SEARCHING AUTHORITY**

|  |  |        |                              |
|--|--|--------|------------------------------|
| Choice of International Searching Authority (ISA)<br>(if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used): | Request to use results of earlier search; reference to that search (if an earlier search has been carried out by or requested from the International Searching Authority): |        |                              |
| ISA / US   | Date (day/month/year)  | Number | Country (or regional Office) |

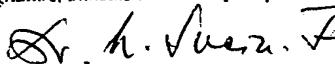
**Box No. VIII CHECK LIST; LANGUAGE OF FILING**

|   |   |  |
|---|---|--|
| This international application contains the following number of sheets: | This international application is accompanied by the item(s) marked below:                                    |  |
| request : 6   | <input checked="" type="checkbox"/> see calculation sheet   |  |
| description (excluding sequence listing part) : 119                     | <input type="checkbox"/> separate signed power of attorney  |  |
| claims : 12   | <input type="checkbox"/> copy of general power of attorney: reference number, if any:                         |  |
| abstract : 1  | <input type="checkbox"/> statement explaining lack of signature   |  |
| drawings : 44   | <input type="checkbox"/> priority document(s) identified in Box No. VI as item(s):                            |  |
| sequence listing part of description : 0                                | <input type="checkbox"/> translation of international application into (language):                            |  |
| Total number of sheets : 182  | <input type="checkbox"/> separate indications concerning deposited microorganism or other biological material |  |
|   | <input type="checkbox"/> nucleotide and/or amino acid sequence listing in computer readable form              |  |
|   | <input checked="" type="checkbox"/> other (specify): Transmittal Letter, Attachment A                         |  |

|   |  |
|---|--|
| Figure of the drawings which should accompany the abstract: | Language of filing of the international application: English |
|---|--|

**Box No. IX SIGNATURE OF APPLICANT OR AGENT**

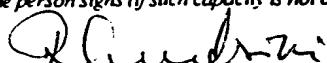
Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).



7/13/2000

Nicole Suciu-Foca

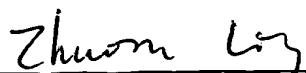
Date



7/13/2000

Raffaello Cortesini

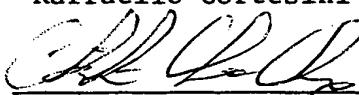
Date



7/13/2000

Zhuoru Liu

Date



7/13/2000

Chih-Chao Chang

Date

For receiving Office use only

|   |  |
|---|--|
| 1. Date of actual receipt of the purported international application:   | 2. Drawings:   |
| 3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application: | <input type="checkbox"/> received:<br><br><input type="checkbox"/> not received:         |
| 4. Date of timely receipt of the required corrections under PCT Article 11(2):  |  |
| 5. International Searching Authority (if two or more are competent): ISA /  | 6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid. |

For International Bureau use only

Date of receipt of the record copy by the International Bureau:

**Supplemental Box**      If the Supplemental Box is not used, this sheet should not be included in the request.

1. If, in any of the Boxes, the space is insufficient to furnish all the information: in such case, write "Continuation of Box No. ..." (indicate the number of the Box) and furnish the information in the same manner as required according to the captions of the Box in which the space was insufficient, in particular:

- (i) if more than two persons are involved as applicants and/or inventors and no "continuation sheet" is available: in such case, write "Continuation of Box No. III" and indicate for each additional person the same type of information as required in Box No. III. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below;
- (ii) if, in Box No. II or in any of the sub-boxes of Box No. III, the indication "the States indicated in the Supplemental Box" is checked: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the applicant(s) involved and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is applicant;
- (iii) if, in Box No. II or in any of the sub-boxes of Box No. III, the inventor or the inventor/applicant is not inventor for the purposes of all designated States or for the purposes of the United States of America: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the inventor(s) and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is inventor;
- (iv) if, in addition to the agent(s) indicated in Box No. IV, there are further agents: in such case, write "Continuation of Box No. IV" and indicate for each further agent the same type of information as required in Box No. IV;
- (v) if, in Box No. V, the name of any State (or OAPI) is accompanied by the indication "patent of addition," or "certificate of addition," or if, in Box No. V, the name of the United States of America is accompanied by an indication "continuation" or "continuation-in-part": in such case, write "Continuation of Box No. V" and the name of each State involved (or OAPI), and after the name of each such State (or OAPI), the number of the parent title or parent application and the date of grant of the parent title or filing of the parent application;
- (vi) if, in Box No. VI, there are more than three earlier applications whose priority is claimed: in such case, write "Continuation of Box No. VI" and indicate for each additional earlier application the same type of information as required in Box No. VI;
- (vii) if, in Box No. VI, the earlier application is an ARIPO application: in such case, write "Continuation of Box No. VI", specify the number of the item corresponding to that earlier application and indicate at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed.

2. If, with regard to the precautionary designation statement contained in Box No. V, the applicant wishes to exclude any State(s) from the scope of that statement: in such case, write "Designation(s) excluded from precautionary designation statement" and indicate the name or two-letter code of each State so excluded.

3. If the applicant claims, in respect of any designated Office, the benefits of provisions of the national law concerning non-prejudicial disclosures or exceptions to lack of novelty: in such case, write "Statement concerning non-prejudicial disclosures or exceptions to lack of novelty" and furnish that statement below.

Continuation of Box V.: U.S. Serial No. 09/333,809, filed June 15, 1999.

## PATENT COOPERATION TREATY

PCT

## NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

|  |   |   |
|--|---|---|
| Date of mailing (day/month/year)<br>21 December 2000 (21.12.00)                  | <i>received</i><br><i>1/15/01</i>                                     |   |
| Applicant's or agent's file reference<br><b>58332-A-PCT/JPW/EMW</b>              | JAN - 2 2001<br>W.D.<br>SOCKET CLEAR                                  |   |
| International application No.<br>PCT/US00/16594                                  | International filing date (day/month/year)<br>15 June 2000 (15.06.00) | Priority date (day/month/year)<br>15 June 1999 (15.06.99) |
| Applicant<br>THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK et al ✓ |   |   |

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:  
AU,KP,KR,MZ,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:  
AE,AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,CA,CH,CN,CR,CU,CZ,DE,DK,DM,EA,EE,EP,ES,FI,GB,GD,  
GE,GH,GM,HR,HU,ID,IL,IN,IS,JP,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MA,MD,MG,MK,MN,MW,MX,  
NO,NZ,OA,PL,PT,RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,TZ,UA,UG,UZ,VN,YU,ZA,ZW  
The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).
3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 21 December 2000 (21.12.00) under No. WO 00/76320

## REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until ~~30 months~~ *1/15/01* *SMB* or later in some Offices from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the ~~19-month time limit~~ *1/15/01* *SMB*.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

## REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the ~~national phase~~, he must, within ~~20 months~~ *2/15/01* or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

|   |                                 |
|---|---------------------------------|
| The International Bureau of WIPO<br>34, chemin des Colombettes<br>1211 Geneva 20, Switzerland | Authorized officer<br>J. Zahra  |
| Facsimile No. (41-22) 740.14.35   | Telephone No. (41-22) 338.83.38 |

## PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION  
(PCT Rule 61.2)

|   |   |
|---|---|
| Date of mailing (day/month/year)<br>08 June 2001 (08.06.01)           | To:<br><br>Commissioner<br>US Department of Commerce<br>United States Patent and Trademark<br>Office, PCT<br>2011 South Clark Place Room<br>CP2/5C24<br>Arlington, VA 22202<br>ETATS-UNIS D'AMERIQUE<br><br>in its capacity as elected Office |
| International application No.<br>PCT/US00/16594                       | Applicant's or agent's file reference<br>58332-A-PCT/JPW/EMW  |
| International filing date (day/month/year)<br>15 June 2000 (15.06.00) | Priority date (day/month/year)<br>15 June 1999 (15.06.99)   |
| Applicant<br>SUCIU-FOCA, Nicole et al                                 |   |

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:  
15 January 2001 (15.01.01)

in a notice effecting later election filed with the International Bureau on:  
\_\_\_\_\_

2. The election  was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

|   |   |
|---|---|
| The International Bureau of WIPO<br>34, chemin des Colombettes<br>1211 Geneva 20, Switzerland<br><br>Facsimile No.: (41-22) 740.14.35 | Authorized officer<br><br>Henrik Nyberg<br><br>Telephone No.: (41-22) 338.83.38 |
|---|---|

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/16594

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : A01N 63/00; C12N 5/02, 5/06, 5/08

US CL : 424/93.71, 810; 435/325, 372.3, 373, 374, 377

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/93.71, 810; 435/325, 372.3, 373, 374, 377

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

DIALOG medicine index; WEST

terms: suppressor, T (cell or lymphocyte), CD8, CD28, autoimmun\$, allograft, xenograft

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category* | Citation of document, with indication, where appropriate, of the relevant passages   | Relevant to claim No. |
|-----------|--|-----------------------|
| X         | JIANG, S. et al. Induction of MHC-class I restricted human suppressor T cells by peptide priming in vitro. Human Immunology. November 1998, Vol. 59, No. 11, pages 690-699, see entire document. | 1-48, 50-56           |

 Further documents are listed in the continuation of Box C. See patent family annex.

|     |   |     |  |
|-----|---|-----|--|
| •   | Special categories of cited documents:  | "T" | later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  |
| "A" | document defining the general state of the art which is not considered to be of particular relevance  | "X" | document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone   |
| "E" | earlier document published on or after the international filing date  | "Y" | document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |
| "L" | document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | "Z" | document member of the same patent family  |
| "O" | document referring to an oral disclosure, use, exhibition or other means  |     |  |
| "P" | document published prior to the international filing date but later than the priority date claimed  |     |  |

Date of the actual completion of the international search

28 AUGUST 2000

Date of mailing of the international search report

15 SEP 2000

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

F. PIERRE VANDERVEGT

Telephone No. (703) 308-0196

**INTERNATIONAL SEARCH REPORT**International application No.  
PCT/US00/16594**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.: 49 because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:  

There is no antecedent basis for the recitation of "MIR" in the claim.
  
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**  

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/16594

## BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

- |  |   |
|--|---|
| Group I, claim(s) 1-3, 9-10, drawn to method of generating   | allospecific human suppressor T cells.                    |
| Group II, claim(s) 4, 11, 27-30, drawn to allospecific human   | suppressor T cells.                                       |
| Group III, claim(s) 5-7, drawn to a method of generating   | xenospecific human suppressor T cells.                    |
| Group IV, claim(s) 8, 31-32, drawn to xenospecific human   | suppressor T cells.                                       |
| Group V, claim(s) 12-13, drawn to a method of determining the therapy given to a patient.  | appropriateness of the level of immunosuppressive         |
| Group VI, claim(s) 14-19, drawn to a method of reducing, patient by the administration of allospecific human suppressor T                | preventing or suppressing allograft rejection in a cells. |
| Group VII, claim(s) 20-22, drawn to a method of reducing, patient by the administration of xenospecific human suppressor T               | preventing or suppressing xenograft rejection in a cells. |
| Group VIII, claim(s) 23-26, drawn to a method for preventing   | autoimmune disease using human suppressor T cells.        |
| Group IX, claim(s) 33-37, drawn to a method for generating   | anergic human T cells.                                    |
| Group X, claim(s) 38-42, drawn to generating tolerogenic antigen   | presenting cells.   |
| Group XI, claim(s) 43-47, drawn to a method of reducing allograft antigen presenting cells.  | rejection by administering tolerogenic                    |
| Group XII, claim(s) 48-52, drawn to a method of suppressing an autoimmune disease by administering tolerogenic antigen presenting cells. |   |
| Group XIII, claim(s) 53-54, drawn to a method of suppressing an autoimmune disease by overexpressing MIR in antigen presenting cells.    |   |
| Group XIV, claim(s) 55, drawn to a method of inducing tolerance antigen presenting cells overexpressing MIR.                             | in an allograft recipient by administering                |
| Group XV, claim(s) 56, drawn to a method of inducing tolerance in antigen presenting cells overexpressing MIR.                           | an xenograft recipient by administering                   |

The inventions listed as Groups I-XV do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the claimed methods of Groups I and III for generating suppressor T cells are drawn to generating cells specific for different targets, allo- versus xeno- specific antigens. The allo- and xeno- specific T cells of Groups II and IV are claimed in a product-by-process manner, but are obtainable by materially different methods. the methods of Groups V-XV are different methods from those of Groups I and III, being a diagnostic method (Group V), a method of generating antigen presenting cells (Group X), and immunosuppressive treatment methods (Groups VI-IX and XI-XV). the groups are not linked by a special technical feature so as to constitute a single inventive concept.